Gly-Gly-Pen, and D-stereoisomers thereof, wherein the first peptide is covalently linked to the second peptide; and

b) detecting gamma radiation emitted by the technetium-99m localized at the site.

R126 5 Canceled

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32. The method of claim 31, further comprising the step of imaging the body using conventional technetium-99m imaging means.

REMARKS

Reconsideration of the application as amended is requested. The specification has been amended to correct typographical errors. No new matter has been added by virtue of the amendments to the specification.

Claims 1-3, 5, 6, 10, and 18-21 have been amended to more specifically point out and distinctly claim the invention as embodied therein. Specifically, claims 1, 2, 3,5, and 6 have been amended to eliminate redundant language. Claim 1 has been further amended to clarify various Markush groupings and to correct the antecedent basis. Claim 2 has been amended to correct spelling. Claims 3, 10, and 18 have been amended to correct the Markush language. Claims 6, 10, and 19 have been amended to correct the dependencies. Claims 19, 20, and 21 have been amended to correct the antecedent basis. Claim 4 has been cancelled in favor of claim 18, and claim 9 has been cancelled and rewritten as new claim 24.

New claims 25 - 33 have been added to provoke interference with the claims of U.S.Pat.No. 5,670,133, as is discussed more fully below. Support for claim 25 appears in the present application at page 7, lines 23-29; at page 8, lines 10-21; at page 9, lines 1-14; at page 11, lines 11-19; at page 12, lines 3-14, 21-25, and 27-28; page 13, line 25 to page 14, line 11; in Table I; in Table IV; and in claims 1, 2, 3, 4, 5, 6, 18, and 19 as filed. Support for claim 26 appears in the present application at page 7, lines 22-29; at page 8, lines 10-21; at page 9, lines 1-14; at page 9, line 25 to page 10, line 1; at page 11, lines 2-19; at page 12, lines 3-14, 21-25, and 27-28; page 13, line 25 to page 14, line26; in Examples 1, 2, 4, 5, 6, and 8; in Table I; in Table IV; in Figure 4; and in claims 7,8, 11, 12, 13, and 22 as filed. Support for claims 27, 28 and 29 appears in the present application at page 9, line26 to page 10, line 1; at page 14, lines 12-26; in Example 2; in Table 1; and in claims 11, 12, 15 and 16 as filed. Support for claims 30 and 31 appears in the present application at page 9, lines 26-29; at page 14, lines 12-19; in Example 1; and in claims 11, 12, 15, and 16 as filed. Support for claims 32 and 33 appears in the present application at page 10, lines 10-14; at page 15. lines 15-29; in Examples 4, 5, 6, and 8; in Figure 4; and in claims 17, 20, and 21 as filed.

No new matter has been added by virtue of the amendments to the claims.

Potentially Interfering Subject Matter of U.S.Pat.No. 5,670,133

Submitted herewith for the Examiner's review is a PTO Form 1449 disclosing U.S.Pat.No. 5,670,133, which issued on September 23, 1997. The claims of U.S.Pat.No. 5,670,133 are directed to a peptide containing a biological-function domain which causes

the peptide to accumulate at a target locus and a metal ion-binding domain comprising an amino acid sequence selected from the group consisting of Gly-Gly-Cys, Gly-Gly-Pen, Gly-Gly-Gly-Cys, and Gly-Gly-Gly-Pen.

The Examiner's attention is directed to new claims 25 through 33, which have been added to provoke an interference with U.S.Pat.No. 5,670,133 as set forth in the Request for Interference Pursuant to 37 C.F.R. 1.607 which is filed herewith. New claim 25 corresponds substantially to claims 1 and 3 of US Pat.No. 5,670,133. New claim 26 corresponds substantially to claims 2, 4, 5, and 6 of US Pat.No. 5,670,133. New claims 27 and 28 correspond substantially to claims 8, 9, 10, 11, 14, 15, and 16 of US Pat. No. 5,670,133. New claims 30 and 31 correspond substantially to claims 14, 15, 16, and 19 of US Pat.No. 5,670,133. New claims 32 and 33 correspond substantially to claims 20 and 21 of US Pat.No. 5,670,133.

Rejection under 35 U.S.C. sec. 112

Claims 1-6, 9, 10, and 19-21 stand rejected under sec. 112, first paragraph. The Examiner takes the position that the scope of "specific binding peptide or compound" is broader than the enabling disclosure, and that undue experimentation would be required to determine the peptides which can recognize any unrestricted component at any unrestricted target site and bind specifically thereto, without guidance to identify and utilize the structure of such peptides or compounds. The Examiner requests a showing

". . . that the instant radionuclides [*sic*] or radiolabeled complexing moieties would deliver said radionuclides or radiolabeled complexing moieties to the site of the target cells." This rejection is respectfully traversed.

In maintaining the instant rejection, the Examiner has in effect questioned the utility of the presently claimed invention, in the guise of a rejection under sec. 112, first paragraph. The Examiner has questioned the credibility of Applicants' statements that the presently claimed reagents have utility for preparing diagnostic imaging agents. No factual basis for questioning Applicants' credibility has been provided, and the instant rejection is based only on the Examiner's opinion.

Applicants note that at col. 9, lines 30-41, U.S.Pat.No. 5,443,816, the patent which issued on USSN 07/840,077, the parent of U.S.Pat.No. 5,670,133, defines "biological function domain" as follows:

> The biological-function domain of the peptide is defined in the specification and claims as a sequence of one or more amino acids which exhibit binding to a biological receptor found on cells, tissues, organs or fluids. The peptides may or may not transmit a signal to the cells, tissues or other materials associated with the biological receptor after binding. The biological-function domain also includes a sequence of one or more amino acids which exhibit binding to a biological receptor found on other peptides, enzymes, antibodies or similar proteinaceous compositions which may themselves exhibit binding to another biological receptor.

U.S.Pat.No. 5,670,133 incorporates the specification of USSN 07/840,077 by reference at col. 9, lines 34-35.

At page 11, lines 11-25, the present application defines "specific binding compound" as follows:

> [f]or purposes of this invention, the term "specific binding compound" is intended to mean any compound that specifically binds to a target site in a mammalian body. "Specific binding" will be understood by those with skill in this art as meaning that the compound localizes to a greater extent

> at the target site that [*sic*, than] to surrounding tissues. Such specific binding is advantageous because scintigraphic imaging agents comprising such specific binding compounds are distributed within a mammalian body after administration to provide visual definition of the target *in vivo*. Specific binding compounds include but are not limited to peptide [*sic*, peptides], oligosaccharides, nucleotides, oligonucleotides and polynucleotides, and specific receptor-binding compounds.
>
> Each specific-binding peptide-containing embodiment of the invention is comprised of a sequence of amino acids. The term amino acid as used in this invention is intended to include all L- and D-, primary α- and β-amino acids, naturally occurring, modified, substituted, altered and otherwise. Specific binding peptide embodiments of the reagents of the invention comprise specific binding peptides having a molecular weight of about 5,000 daltons.

It is clear that the biological function domain of the peptides of U.S.Pat.Nos. 5,443,816 and 5,670,133 is substantially the same as the specific binding peptide of the present application. It is also clear that claims containing the term "biological-function domain" were allowed in U.S.Pat.Nos. 5,443,816 and 5,670,133, without further definition of structure or binding specificity. Other examiners within the Patent and Trademark Office have thus not agreed with the present Examiner's opinion regarding the credibility of generic claim terms similar to the present "specific binding compound or peptide".

Applicants have shown that identifying and assaying a specific binding compound is a matter of ordinary skill. Moreover, the Patent and Trademark Office has acknowledged this fact by issuing U.S.Pat.Nos. 5,443,816 and 5,670,133. In Example 1 of the present application, Applicants have taught how to establish a covalent linkage between a specific binding compound, in particular, a specific binding peptide, and a radiolabel complexing moiety of formula I or formula II. In Example 2, Applicants have shown that reagents within the scope of the present claims can be radiolabeled. In Example 3, Applicants have shown that reagents within the scope of the present claims

maintain their binding specificity after a radiolabel complexing moiety has been added to a specific binding peptide. The remaining examples of the application demonstrate utility of the reagents within the scope of the present claims for preparing imaging agents for a variety of indications: imaging deep vein thrombosis, imaging atherosclerotic plaque, imaging infection, and imaging somatostatin receptor expressing tumors.

In fact, as indicated in the attached Declaration of John Lister-James Pursuant to 37 C.F.R. sec. 1.132, several compounds within the scope of the present claims have been studied in human clinical trials. One compound disclosed in the present application has completed clinical trials and is currently under review by the Food and Drug Administration for imaging deep vein thrombosis. Another compound within the scope of the present claims has completed clinical trials and a New Drug Application is presently being prepared by Applicants' assignee.

No factual basis exists for the Examiner's doubt of the objective truth of Applicants' statements in the present application. In light of the above, withdrawal of the rejection of claims 1-6, 9, 10, and 19-21 is respectfully requested.

Claim 18

No rejection is pending against claim 18, which claims a number of specific peptide reagents. Allowance of claim 18 is therefore respectfully requested.

In light of the amendments and arguments set forth above, Applicants submit that the rejection contained in the final Office Action of October 29, 1997 should be withdrawn and that the present claims are in condition for allowance or appeal. Should the Examiner wish to discuss this application further, she is requested to contact the undersigned attorney.

Respectfully submitted,

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